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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/568,055	09/27/2006	Aidan Doherty	6947-73362-01	3696

24197 7590 03/15/2010

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EXAMINER	
HUTSON, RICHARD G	
ART UNIT	**PAPER NUMBER**
1652	

MAIL DATE	DELIVERY MODE
03/15/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/568,055	DOHERTY ET AL.	
	Examiner	Art Unit	
	Richard G. Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 November 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5,8,10-21,23-27,31 and 34-43* is/are pending in the application.

4a) Of the above claim(s) *15-17, 24-27 and 34-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,8,10-14,18-21,23 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's cancellation of claims 2-4, 6, 7, 9, 22, 28-30, 32-33 and the amendment of claims 1, 5, 8, 15, 18, 21, 24-26, 31, 34, 35 in the paper of 11/30/2009, is acknowledged. Claims 1, 5, 8, 10-21, 23-27, 31, 34-43 are still at issue and are present for examination.

Claims 15-17, 24-27 and 34-43 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Specification

The disclosure is objected to because of the following informalities:

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth: The following portions of the specification list sequences which appear to meet the definition for a nucleic acid sequence, but do not have an associated SEQ ID No: Figure 12.

Applicants traverse this requirement on the basis that applicants submit that the sequence in Figure 12 do not require associated sequence identifiers on the basis "that none of these sequences are more than 10 nucleotides in length". Applicants submit that unless a sequence is more than 10 nucleotides in length, inclusion of a corresponding sequence identifier is not required. Applicants point to Slide 8 of the presentation presented by Robert Wax at the Biotechnology, Chemical &

Pharmaceutical Customer Partnership Meeting in 2009 and 37 CFR 1.82(a) and MPEP 2422.03.

Applicants complete argument is acknowledged but is not found persuasive on the basis that slide 8 of the presentation that Applicants refer to says "The inclusion of sequences containing fewer than (4) specifically defined amino acids or (10) nucleotides (four specifically defined) is not mandatory"

Applicants referred to nucleotide sequences contain 10 nucleotide sequences, not "fewer than 10 nucleotides". Further

> 37 CFR 1.821. Nucleotide and/or amino acid sequence disclosures in patent applications. (a) Nucleotide and /or amino acid sequences as used in § § 1.821 through 1.825 are interpreted to mean an unbranched sequence of four or more amino acids or an unbranched sequence of **ten or more nucleotides**.

As applicants referred to nucleotide sequence of Figure 12 comprise ten nucleotides and ten is included in ten or more and they are thus included in those sequences requiring a sequence identifier.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 5, 8, 10-14, 18-21, 23 and 31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection was stated in the previous office action as it applied to previous claims 1-14, 18-23 and 28-33. In response to this rejection applicants have cancelled claims 2-4, 6, 7, 9, 22, 28-30, 32-33 and amended claims 1, 5, 8, 15, 18, 21, 31 and traverse the rejection as it applies to the newly amended claims.

Applicants traverse this rejection on the basis that applicants submit that they have amended claims 1, 8, 15, 18 and 21 to include recite "wherein the prokaryotic DNA ligase polypeptide comprises an amino acid sequence having at least 95% sequence identity to the amino acid sequence of accession number CAB08491 (SEQ ID NO:91). Applicants submit that because the claims are no longer directed to *any* prokaryotic DNA ligase polypeptide, Applicants believe that this rejection is moot and withdrawal of the instant rejection is respectfully requested.

Applicants submit that in the instant case, the amended specification provides SEQ ID NO: 91, which is a member of the genus of prokaryotic DNA ligase polypeptides comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of accession number CAB08492 (SEQ ID NO: 91). Applicants submit that the specification provides information regarding the structure of SEQ ID NO: 91, for

example, Figure 4 shows a domain map of CAB08491 (SEQ ID NO: 91) that highlights conserved motifs and Table 2 shows conserved motifs of prokaryotic ligases with key conserved residues within those motifs (see Table 2 and description of Table 2 on page 16 of the specification). Thus, applicants submit that the specification provides a member of the claimed genus, and also provides structural information regarding members of the claimed genus.

Applicants further submit that additionally, structural information regarding ATP-dependant DNA ligases˜ was known to those of skill in the art as of the priority date of the instant application .

Applicant's amendment of the claims and applicants complete argument is acknowledged and has been carefully considered, however, is found non-persuasive for the reasons previously made of record and for those reasons provided herein.

With regard to applicants submission that they have amended claims 1, 8, 15, 18 and 21 to include recite "wherein the prokaryotic DNA ligase polypeptide comprises an amino acid sequence having at least 95% sequence identity to the amino acid sequence of accession number CAB08491 (SEQ ID NO:91), it is pointed out to applicants that applicants continue to claim a method of modifying a nucleic acid comprising the use of a DNA ligase polypeptide which comprises an amino acid sequence having at least 95% sequence identity to the amino acid sequence of accession number CAB08491 (SEQ ID NO: 91). These claims continue to encompass the use of any DNA ligase polypeptide which comprises an amino acid sequence, which

includes fragments of an amino acid sequence that has 95% identity to the amino acid sequence of SEQ ID NO:91. For this reason while applicants have amended the claims such that they do not read on the use of any DNA ligase polypeptide, it continues that they are not draw to the use of DNA ligases which have 95% amino acid sequence identity to SEQ ID NO:91. It is this considerably broader genus of methods of use of a DNA ligase polypeptide that remain inadequately described.

The information that applicants specification provides regarding the structure of SEQ ID NO: 91, for example, Figure 4 shows a domain map of CAB08491 (SEQ ID NO: 91), that highlights conserved motifs and Table 2 shows conserved motifs of prokaryotic ligases with key conserved residues within those motifs (see Table 2 and description of Table 2 on page 16 of the specification) is insufficient to describe the considerably broader genus of DNA ligase polypeptides used in the claimed methods.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1, 5, 8, 10-14, 18-21, 23 and 31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of ligating nucleic acid molecule ends comprising contacting that ligase isolated from *Mycobacterium tuberculosis* and having the amino acid sequence of SEQ ID NO:91, does not reasonably provide enablement for any method of modifying a nucleic acid molecule comprising contacting the nucleic acid molecule with any prokaryotic DNA

ligase polypeptide comprising an amino acid sequence having 95% sequence identity to the amino acid sequence of SEQ ID NO:91. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

This rejection was stated in the previous office action as it applied to previous claims 1-14, 18-23 and 28-33. In response to this rejection applicants have cancelled claims 2-4, 6, 7, 9, 22, 28-30, 32-33 and amended claims 1, 5, 8, 15, 18, 21, 31 and traverse the rejection as it applies to the newly amended claims.

Applicants traverse this rejection on the basis that the test for enablement does not hinge on predictability, but rather on whether or not the specification teaches one of skill in the art how to make and use the invention without undue experimentation. *In re Wands',* 858 F.2d 731,737 (Fed.Cir.1988); *Genentech, Inc. v. Novo Nordisk,* 108 F.3d 1361, 1365 (Fed.Cir. 1997).

Applicants submit that application of the Wands factors to the instant case supports a conclusion that the claims are enabled. For example, while the present invention is in the field of molecular biology, which is a field believed to be somewhat unpredictable, the level of skill in this field is high. Applicants submit that the techniques required to practice the invention were well known to those of skill in the art.

Applicants submit that the state of the art of protein engineering at the time of the invention was advanced. At the time of the invention, for example, *in silico* techniques were commonplace for the identification and modeling of secondary and

tertiary protein structures, and variant sequences at least 95% identical to SEQ ID NO: 91 that were suitable for use in the claimed methods could be identified easily, given the teaching in the specification regarding the conserved motifs of the protein. This is not reflected in the references cited by the Examiner *(e.g.,* Ngo *et al.),* which were published years before the priority date of the application.

Further, applicants submit that the amended claims are limited to the use of polypeptide sequences that have at least 95% sequence identity to SEQ ID NO: 91.

Applicants submit that similarly in *Kubin the examiner* had asserted that the art was unpredictable and despite this, the Board found the claim to be enabled when all of the *Wands'* factors were considered. In the instant case, the 95% sequence identity threshold, coupled with the fact that the level of skill in the instant field is high and the general techniques required to practice the invention were well known to those of skill in the art at the time of Applicants' filing, support a finding that the amount of experimentation required to make and use the full breadth of the method of claims 1-14, 18-23 and 28-33 is not undue.

Applicant's amendment of the claims and applicants complete argument is acknowledged and has been carefully considered, however, is found non-persuasive for the reasons previously made of record and for those reasons provided herein.

With regard to applicants submission Applicants have met each of the factors stated in the Wands analysis: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working

examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s), it is acknowledged that the test for enablement does not hinge on predictability, but rather on whether or not the specification teaches one of skill in the art how to make and use the invention without undue experimentation. *In re Wands',* 858 F.2d 731,737 (Fed.Cir.1988); *Genentech, Inc. v. Novo Nordisk,* 108 F.3d 1361, 1365 (Fed.Cir. 1997).

While the present invention is in the field of molecular biology, which is a field believed to be somewhat unpredictable, the level of skill in this field is high and it is acknowledged that the techniques required to practice the invention were well known to those of skill in the art.

The Wands factor that applicants have not accurately addressed is that which is most critical for applicant's claims, the breadth of the claim(s).

As above, with regard to applicants submission that they have amended claims 1, 8, 15, 18 and 21 to include recite "wherein the prokaryotic DNA ligase polypeptide comprises an amino acid sequence having at least 95% sequence identity to the amino acid sequence of accession number CAB08491 (SEQ ID NO:91), it is pointed out to applicants that applicants continue to claim a method of modifying a nucleic acid comprising the use of a DNA ligase polypeptide which comprises an amino acid sequence having at least 95% sequence identity to the amino acid sequence of accession number CAB08491 (SEQ ID NO: 91). These claims continue to encompass

the use of any DNA ligase polypeptide which comprises an amino acid sequence, which includes fragments of an amino acid sequence that has 95% identity to the amino acid sequence of SEQ ID NO:91. For this reason while applicants have amended claims do not read on the use of any DNA ligase polypeptide, it continues that they are not draw to the use of DNA ligases which have 95% amino acid sequence identity to SEQ ID NO:91, but to the considerably broader genus of those methods of use of any DNA ligase polypeptide comprising an amino acid sequence which has at least 95% amino acid sequence identity to SEQ ID nO:91. It is this considerably broader genus of methods of use of a DNA ligase polypeptide that remain are at the heart of the lack of scope of enablement of the claimed genus of methods.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of nucleic acid modifications comprising the use of any prokaryotic DNA repair ligase polypeptide. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of those methods and required polypeptides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Mahajan et al. (U.S. Patent No. 5,976,806) as evidenced by Srivastava et al. (Journal of Biological Chemistry, Vol. 280, No. 34, pp 30273-30281, 2005).

This rejection was stated in the previous office action as it applied to previous claims 1, 2 and 4. In response to this rejection applicants have amended claim 1 and cancelled claims 2 and 4 and traverse the rejection as it applies to the newly amended claims.

Applicants traverse this rejection on the basis that applicants submit that they have amended claim 1 such that it is limited to a method of modifying a nucleic acid molecule comprising contacting the nucleic acid molecule with an isolated prokaryotic DNA ligase polypeptide, wherein the prokaryotic DNA ligase polypeptide comprises an amino acid sequence having at least 95% sequence identity with the amino acid sequence of accession number CAB08492 (SEQ ID NO: 91). Applicants submit that the '806 patent does not disclose the sequence of CAB08492 (SEQ ID NO: 91) or any polypeptide having at least 95% sequence identity with CAB08492 (SEQ ID NO: 91).

Applicant's amendment of claim 1 and applicant's complete argument are acknowledged and have been carefully considered, however, are not found persuasive on the following basis. While it is acknowledged that that the '806 patent does not disclose the sequence of CAB08492 (SEQ ID NO: 91), the '806 patent does disclose an isolated prokaryotic DNA ligase polypeptide, wherein the prokaryotic DNA ligase polypeptide "comprises **an** amino acid sequence" having at least 95% sequence identity with the amino acid sequence of accession number CAB08492 (SEQ ID NO: 91). Applicants are reminded that rejected claim 1 is drawn to a method of use of a DNA ligase polypeptide which comprises an amino acid having at least 95% sequence identity to CAB08492 (SEQ ID NO:91) and this includes fragments of CAB08492 (SEQ ID NO:91). Further it is not required that the amino acid sequence that has 95% sequence identity with CAB08492 also have activity, but rather the larger DNA ligase polypeptide that comprises this sequence must have the ligase activity.

Thus claim 1 remains rejected by Mahajan et al. (U.S. Patent No. 5,976,806) as evidenced by Srivastava et al. (Journal of Biological Chemistry, Vol. 280, No. 34, pp 30273-30281, 2005).

Remarks

No claim is allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is 571-272-0930. The examiner can normally be reached on M-F, 7:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

rgh
3/11/2010

/Richard G Hutson/
Primary Examiner, Art Unit 1652